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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPEAL BRIEF
FOR APPELLANTS

James M. Coull
Henrik Stender
Brian D. Gildea

Methods And Compositions For Sorting And/Or Determining Organisms

Serial No.: 09/996,658
Confirmation No.: 5256
Filed: November 29, 2001
Group Art Unit: 1634
Appeal No.:

The attached Appeal Brief is submitted in accordance with the Notice of Appeal mailed on September 20, 2005. Enclosed herewith is a petition under 37 C.F.R. § 1.136(a) for a four-month extension of time as well as authorization for payment of the appropriate fee. Furthermore, The Office is authorized to deduct the appropriate fee, believed to be $ 500.00, under 37 C.F.R. § 40.20(b)(2) for consideration of this Appeal Brief from Deposit Account 01-2213. No other fees are believed to be due for the filing of this paper but if The Office disagrees, The Office is authorized to deduct the appropriate fee from Deposit Account 01-2213.

Respectfully submitted,

March 13, 2006
Date:

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Appeal Brief

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re the application of: Appeal No.

Coull et al. Examiner: Bradley L. Sisson

Serial Number: 09/996,658 Group Art Unit: 1634

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For: Methods And Compositions For Sorting And/Or Determining Organisms

BRIEF ON APPEAL

March 13, 2006

INTRODUCTION

This is an appeal from the action of the Examiner dated April 20, 2005, finally rejecting claims 1-50, all of the claims pending in this application. According to said Office Action, claims 1-50 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Claims 1-50 also stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. No claim stands allowed.

A Notice of Appeal was timely filed on September 20, 2005 (along with an appropriate request for an extension of time under 37 C.F.R. § 1.136(a)). A petition under 37 C.F.R. § 1.136(a) for an automatic four-month extension of time is being filed with this Appeal Brief and therefore it is believed that this Appeal Brief is timely filed. Accordingly, please consider this Brief on Appeal.

1. REAL PARTY IN INTEREST

The application has been assigned to Boston Probes, Inc., 15 DeAngelo Drive, Bedford, MA. USA. As of the filing of this Brief on Appeal, Boston Probes, Inc. is wholly owned by Applera Corporation, acting through its Applied Biosystems stock group. These stand as the parties having an interest herein.

2. STATEMENT OF RELATED APPEALS AND INTERFERENCES

To the best of the knowledge of Appellants' legal representative and the assignee, no related appeals, interferences and/or judicial proceedings are pending.

3. STATUS OF CLAIMS

Claims 1-50 stand rejected. Appellants appeal the rejection of all claims.

4. STATUS OF AMENDMENTS

All amendments of record appear to have been entered. The claims set forth in Section 8 (Claims Appendix) reflect the entry of all amendments. No new amendments are offered.

5. SUMMARY OF THE INVENTION

The presently claimed invention pertains to methods for sorting and/or determining organisms (Title).

(*Independent Claim 1*)

In some embodiments, this invention is directed to a method comprising treating a sample, or a portion thereof, with at least one detectable molecular probe wherein the molecular probe or probes are selected such that either: (i) both the organism of interest and the other organism or organisms react with the molecular probe in a way that produces detectable organisms of interest and a detectable other organism or organisms to be distinguished; or (ii) only the

organism of interest reacts with the molecular probe in a way that produces only detectable organisms of interest. According to the method, the sample, or a portion thereof, is also contacted with a solid carrier to which has been immobilized a binding partner such that if (i) applies then the binding partner is chosen to be reactive only with the detectable organism of interest but not reactive with the detectable other organism or organisms to be distinguished; but if (ii) applies then the binding partner is chosen to be generally reactive with the detectable organism of interest but also may be reactive with the other organism or organisms to be distinguished. Once the organisms have been stained and immobilized to the solid carrier, the method involves determining the presence, absence, position or number of detectable organisms immobilized to the solid carrier and correlating the result with the presence, absence, or number of the organisms of interest in the sample, or portion thereof. (Specification at page 22, lines 12-30)

(*Independent Claim 18*)

In some embodiments, this invention is directed to a method comprising treating a sample, or a portion thereof, with one or more detectable or independently detectable molecular probes wherein the one or more molecular probes are selected such that either: (i) the detectable probe or probes react with the different organisms to be determined in a way that produces different detectable organisms that possess the same stain; or (ii) the independently detectable probes react with the different organisms to be determined in a way that produces different independently detectable organisms that possess an independently detectable stain. According to the method, the sample, or a portion thereof, is also contacted with one or more different types of coded beaded supports, wherein each different type of coded beaded support can be independently determined in a suitable particle sorter and wherein to each different type of coded beaded support has been immobilized a particular binding partner that is chosen to select a particular organism or organisms such that detectable or independently detectable organisms become selectively bound to

the coded beaded supports as a result of the occurrence of specific binding partner interactions. According to the method, the different types of coded beaded supports are then sorted in a suitable particle sorter. The presence, absence, or number of the detectable organism or organisms, or each of the independently detectable organisms, immobilized to each different type of coded beaded support is also determined. This result is then either: (iii) correlated with the code that is associated with a particular immobilized binding partner to thereby determine the presence, absence or number of each of the different organisms of interest in the sample or portion thereof; or (iv) correlated with the code for a sample source from which the sample, or portion thereof, was derived to thereby determine the presence, absence or number of each of the different organisms of interest in each different sample, or portion thereof. (Specification at page 25, lines 3-28).

(*Independent Claim 35*)

In some embodiments, this invention is directed to a method comprising treating a sample, or a portion thereof, with one or more detectable or independently detectable molecular probes wherein the one or more molecular probes are selected such that either: (i) the detectable probe or probes react with the different organisms to be determined in a way that produces different detectable organisms that possess the same stain; or (ii) the independently detectable probes react with the different organisms to be determined in a way that produces different independently detectable organisms that possess an independently detectable stain. According to the method, the sample, or a portion thereof, is contacted with a solid carrier array to which binding partners have been immobilized at unique, identifiable locations such that the detectable or independently detectable organisms are selectively bound to the locations on the array as a result of the occurrence of specific binding partner interactions. The presence, absence or number of the detectable or independently detectable organisms immobilized at the many different locations of the array is then determined and the result is correlated with the particular binding partner

immobilized to each location on the array to thereby determine the presence, absence or number of the different organisms of interest in the sample. (Specification at page 30, lines 1-18)

6. CONCISE STATEMENT OF THE REJECTIONS TO BE REVIEWED

Claims 1-50 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Claims 1-50 also stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. The rejections are of the blanket type as the patentability of individual claims has apparently not been independently considered.

All rejections under 35 U.S.C. § 112, first paragraph are respectfully traversed. The issue on Appeal is whether or not each of these pending rejections is proper. Appellants request that The Board overrule the Examiner and withdraw the rejections.

7. APPELLANT'S ARGUMENTS

A. The Examiner's "Objection" To "Incorporation By Reference"

Although not an express rejection of the claims, paragraph 2 of the Office Action dated April 20, 2005 (hereinafter the "Final Action") appears to suggest that the information asserted to be incorporated by reference in the specification is necessary to meet the enablement and/or written description requirements of 35 U.S.C. § 112, first paragraph (*c.f.* the rejections and comments in paragraphs 4-13 of the Final Action). Appellants disagree with this assertion and discuss this "objection" because the present rejections under 35 U.S.C. §112, first paragraph appear to rely heavily on this presumption. Appellants believe that this issue is a "red herring" since its resolution is irrelevant to the issue of whether or not a skilled artisan can practice the claimed invention based upon the content of the present disclosure and the knowledge available in the art.

With reference to Section V (page 15-16) of Appellant's submission dated September 20, 2005, Appellants commented that any reliance on "*Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2004) 54 USPQ2d at 1679 (hereinafter "*Advanced Display Systems*") to reject claim 1-50 is misplaced. In particular, *Advanced Display Systems* considered the question of whether or not a prior art reference anticipates the claimed subject matter of a later filed patent application under 35 U.S.C. § 102 depending upon whether or not certain information has been properly incorporated by reference. Since the present claims are not rejected under 35 U.S.C. § 102, any reliance on this decision to support the present rejection under 35 U.S.C. §112 would be improper.

Reference is also made to the first continuation sheet associated with the Advisory Action dated October 28, 2005 (hereafter the "Advisory Action"). The top of said continuation refers to "*Ex parte Raible*, 8 USPQ2d 1707 (BPAI, 1998). Appellants' representative was unable to find a copy of *Ex parte Raible* since 8 USPQ2d 1707 appears to the citation to: *Water Technologies Corporation, Water Pollution Control Systems, Inc. and Kansas State University Research Foundation v. Calco Ltd. and William Gartner*. Because Appellants are without a copy of this newly cited caselaw (first cited in the Advisory Action and not the Final Action), Appellants cannot directly respond. **Accordingly, Appellants request that the Examiner immediately either correct the citation else provide Appellants with a copy of the *Raible* decision upon which he is relying in support of his maintaining the present rejections.**

Regardless, the quote asserted to be from *Raible*, cites to *In re de Seversky*, 474, F.2d 671, 177 USPQ 144 (CCPA, 1973) (hereinafter "*Seversky*"). Like *Advanced Display Systems*, *Seversky* does not address the situation where claims have been rejected under 35 U.S.C. § 112, first paragraph. Rather, the question presented in *Seversky* is whether or not an applicant can antedate a reference by incorporation by reference of a related earlier filed application to overcome a rejection under 35 U.S.C. § 103. Since the present claims are not

rejected under 35 U.S.C. § 103, again any reliance on this decision to support the present rejection under 35 U.S.C. §112 would be improper.

Regardless of the foregoing, it is well accepted that: "*To satisfy the written description requirement a patent specification must describe the claimed invention in sufficient detail that* ***one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention***" (emphasis added) M.P.E.P. § 2163(I). "*Information which is well known in the art need not be described in detail in the specification*" M.P.E.P. § 2163(II)(A)(2).

Accordingly, the determination of written description and/or enablement is viewed in light of the knowledge attributable to the ordinary practitioner. Thus, it is not necessary to incorporate by reference text from a printed patent or publication to thereby comply with the written description or enablement requirements of 35 U.S.C. § 112, first paragraph since this knowledge is imputed to the ordinary practitioner. For example, in the *Advanced Display Systems* and *Seversky* the references were found to be part of the knowledge of one of skill in the art thereby resulting in the denial of a valid patent. The Examiner has even stated that: "an applicant may utilize bibliographical citations in the application's specification so to establish the level of skill in the art and/or state of the art at the time of filing." (Advisory Action at continuation sheet page 1, paragraph 4) Accordingly, Appellants believe that the "objection" is irrelevant to the basis of the present rejections and that to the extent that the Office believes that *Advanced Display Systems* and *Seversky* support these rejections under 35 U.S.C. §112, first paragraph, Appellants simply argue that these decisions are off-point and irrelevant and that any rejection based thereon must be improper.

B. Rejection Under 35 U.S.C. § 112, First Paragraph For Lack Of Written Description

(a) The Law

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." M.P.E.P. § 2163 (I)(A). The examiner, therefore, must therefore have a reasonable basis to challenge the adequacy of the written description". M.P.E.P. § 2163.04 In rejecting a claim, the examiner must set forth express findings of fact which support the lack of written description conclusion..." M.P.E.P. § 2163.04(I).

"The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed...." M.P.E.P. § 2163(II)(A)(2) "Information which is well known in the art need not be described in detail in the specification." *Id.*

"To satisfy the written description requirement a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention." M.P.E.P. § 2163(I) An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Id.*

(b) Analysis of The Rejections In View Of The Law

(i) The Claimed Invention And All Of Its Limitations Are Disclosed In The Specification

As stated above, the there is strong presumption that an adequate written description of the claimed invention is present when the application is filed.

Therefore the examiner bears a heavy burden in setting forth express findings of fact that support a determination that the specification lacks a proper written description. Absent a proper finding of fact, Appellants are entitled to their patent.

As is evident from a review of the specification, all of the limitations of the claimed subject matter are discussed in the specification with reference to the knowledge of the ordinary practitioner. For example, elements of method claim 1 include "organism of interest" (discussed in the specification, *inter alia*, at page 19, lines 10-21), "detectable molecular probe" (discussed in the specification, *inter alia*, at page 7, lines 24 to page 8, line 2 and the discussion of "nucleic acid" and "non-nucleic acid polymers" in the definitions section (pages 7-10 as well as the related discussion of the synthesis, labeling, hybridizing and detecting hybridization of said probes to target sequences at pages 7-19), "solid carrier" (discussed in the specification, *inter alia*, at page 10, lines 20-28, page 3, line 19 to page 4, line 5 as well as at page 19, line 22 to page 21, line 30) and "binding partner" (discussed in the specification, *inter alia*, at page 10, lines 10-19, page 3, lines 11-17, line 5 as well as at page 21, lines 15-30).

Appellants also note that the present situation differs significantly from the facts in either of *Advanced Display Systems* and *Seversky* since, in the present case, all elements of the claimed subject matter are described within the four corners of the specification.

Since Appellants have demonstrated possession of the claimed invention by describing the claimed invention with all of its limitations within the four corners of the specification, it is clear that any assertion that they have not is clear error.

(ii) The Findings of Fact are Deficient

With respect to the Final Action, after; 1) citing to "*University of Rochester v G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428" (hereinafter "*Rochester*") at paragraph 4; 2) reproducing an image of independent claims 1, 18 and 35 from the record at paragraph 5; and 3) providing an interpretation of

the claims at paragraph 6 of the Office Action, the Examiner concludes that: "*A review of the specification fails to find adequate written description of any molecular probe and binding partner that are to be used in the claimed invention.*" (Final Action at paragraph 7, page 8) This asserted finding of fact is not correct.

The term "molecular probe" is defined in the specification at page 7 as:

> *"...a nucleic acid or non-nucleic acid polymer (e.g. a DNA, RNA, PNA, nucleic acid analogs, nucleic acid mimics, chimera or linked polymer) having a probing nucleobase sequence that is designed to sequence specifically hybridize to a target sequence of a target molecule of an organism of interest."* (Specification at page 7)

The term "binding partner" is also defined in the specification at page 10 as:

> *"...those molecules that bind to one or more other molecules in a specific manner. Because the binding partner interactions are specific, there is a degree of selectivity that is achieved depending on the nature of the binding partners chosen. Non-limiting examples of binding partner complexes (formed from the component binding partners) include antibody/antigen interactions, nucleic acid/nucleic acid interactions, enzyme/substrate interactions and receptor/ligand interactions. A non-limiting list of ligands includes avidin (and its analogs such as Streptavidin and Lumavidin™), lectins, carbohydrates, peptides and proteins. The preferred pair of binding partners used in the practice of this invention is the antibody/antigen."* (Specification at page 10)

The terms "nucleic acid", "non-nucleic acid", "target sequence", "antibody", and "peptide nucleic acid" are also defined in the definitions section of the specification (pages 7-10). Further reference is made to Example 1.

The terms "binding partner" and "molecular probe", being exemplified by well-known and understood compositions, provide the ordinary practitioner with sufficient information to understand that Applicant possesses and has adequately described the present invention. For example, References **CS** (*Evaluation of a Fluorescent-Labelled Oligonucleotide Probe Targeting 23S rRNA for In Situ Detection of Salmonella Serovars in Paraffin-Embedded Tissue Section and Their*

Rapid Identification in Bacterial Smears), **DC** (*Differentiation of Mycobacterium tuberculosis Complex and Nontuberculous Mycobacterial Liquid Cultures by Using Peptide Nucleic Acid-Fluorescence In Situ Hybridization Probes*), **DE** (*Filter-based PNA in situ hybridization for rapid detection, identification and enumeration of specific micro-organisms*), **DF** (*Differentiation of Candida albicans and Candida dubliniensis by Fluorescent In Situ Hybridization with Peptide Nucleic Acid Probes*), **DH** (*Use of PNA oligonucleotides for the in situ detection of Escherichia coli in water*) **DI** (*Combination of ATP-bioluminescence and PNA probes allows rapid total counts and identification of specific microorganisms in mixed populations*), **DJ** (*Direct detection and identification of Mycobacterium tuberculosis in smear-positive sputum samples by fluorescence in situ hybridization (FISH) using peptide nucleic acid (PNA) probes*), **DL** (*Identification of Dekkera brusellensis (Brettanomyces) from Wine by Fluorescence In Situ Hybridization Using Peptide Nucleic Acid Probes*) and **DO** (*In Situ Hybridization of Prochlorosoccus and Synechococcus (Marine Cyanobacteria) ssp. With rRNA-Targeted Peptide Nucleic Acid Probes*) all contain detailed discussions of the use of peptide nucleic acid probes as a "molecular probe" for the determination of a diverse variety of organisms such as *Salmonella Serovars* bacteria, *Mycobacterium tuberculosis* and non-tuberculous mycobacteria, *Candida albicans and Candida dubliniensis* yeast, *Escherichia coli* bacteria, *Dekkera brusellensis (Brettanomyces)* yeast *and Prochlorosoccus and Synechococcus (Marine Cyanobacteria)* picoplankton. Similarly, References, **DS** (*Simultaneous detection of cucumber mosaic virus, tomato mosaic virus and potato virus Y by flow cytometry*), **DT** (*Identification of pathogenic agents via microsphere – based immunoassays on a flow cytometer*) and **DU** (*Rapid and sensitive detection of Salmonella (O:6,7) by immunomagnetic monoclonal antibody-based assays*) demonstrate the application of antibodies/antigens as binding partners that can be used to determine a diverse variety of organisms such as *cucumber mosaic virus, tomato mosaic virus, potato virus Y, MS2 bacteriophage or Salmonella*

(O:6,7). Furthermore, Reference **DB** (*Combination of rRNA-targeted Hybridization Probes and Immuno-Probes for the Identification of Bacteria by Flow Cytometry*) suggests combining both molecular probes (i.e. nucleic acid probes) and "immuno-probes" (i.e. antibody/antigen interactions) for the determination of micro-organisms and further states:

> *"This combination of rRNA-targeted hybridization probes and immuno-probes for flow cytometry makes possible the highly specific and automated identification of micro-organisms at any desired taxonomic level"* (emphasis added, Reference **DB**, under the heading "Summary" on page 569)

Therefore, from these references it is clear that molecular probes and binding partners are well-known compositions that exhibit specific and reasonably predictable binding properties utilized to determine micro-organisms. Accordingly, because the asserted facts upon which this rejection relies are clearly erroneous, the rejection should be withdrawn for lack of factual support.

(iii) The Specification & References Supply Facts

In rebuttal to Appellants' filing of January 6, 2005, the Final Action simply stated:

> *"At pages 3-9 of the response to the Office action mailed 27 July 2004 applicant's representative **offers opinion** as to what is well known in the art, to what degree a skilled artisan would interpret the description provided, as well as **opinion statements** as to what is within the level of skill of the ordinary artisan."* (emphasis added, Final Action at page 11-12)

followed by a quotation from MPEP § 2145. It is respectfully submitted that such a terse response is both inaccurate and incomplete. What the specification teaches is a matter of fact.[1] What a reference teaches is also a matter of fact. *In*

1 See: *In re Wiseman*, 596 F.2d 1019, 1023, 201 U.S.P.Q. 658, 661 (C.C.P.A. 1979) where the

re Bell, 991 F.2d 781, 784, 26 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1993). More importantly, it is clearly error to tersely dismiss statements made by the Appellants' attorney[2] with reference to the content of the specification as "opinion". Failure to properly consider the content of any Reference or the specification referred to in counsel's argument is itself evidence of the Office's failure to acknowledge the state of the art which is itself reversible error.

(iv) Assertions re Obviousness are Misleading, Incomplete and Erroneous

At paragraph 8 of the Final Action, there is a short quote from the decision in "*University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 41 USPQ2d at 1405" (hereinafter "*Lilly*"), before it is concluded that obviousness cannot be relied upon for satisfaction of the written description requirement (OA at paragraph 8, page 8). Importantly, there is no analysis whatsoever of how Appellants have supposedly attempted to rely upon obviousness for compliance with the written description requirement.

Regardless, it is respectfully submitted that the quotation is misleading. The full text of the quoted paragraph reads:

> *"As indicated, Example 6 provides the amino acid sequence of the human insulin A and B chains, but that disclosure also fails to describe the cDNA.* ***Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.*** *Lockwood, 107 F.3d at 1572, 41 U.S.P.Q.2D (BNA) at 1966. We had previously held that a claim to a specific DNA is not made obvious by mere knowledge of a desired protein sequence and methods for generating the DNA that encodes that protein. See, e.g., In re Deuel, 51 F.3d 1552, 1558, 34 U.S.P.Q.2D (BNA) 1210, 1215 (1995) ("A prior art disclosure of the amino acid*

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court looks to the specification for support regarding Appellant's claim to unexpected results. Moreover, the court in *In re Schulze* looked to the specification for support of a claim to unexpected results by stating: "Nor do we find anything in the record by way of **disclosure** (emphasis added) or affidavit ..." (*In re Schulze*, 52, C.C.P.A. 1422, 1424, 346 F.2d 600, 602, 145 U.S.P.Q. 716, 718 (C.C.P.A. 1965)

2 Attorney Gildea is also an identified inventor of the claimed subject matter.

*sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein."); In re Bell, 991 F.2d 781, 785, 26 U.S.P.Q.2D (BNA) 1529, 1532 (Fed. Cir. 1993). Thus, a fortiori, a description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of § 112, P 1. Because the '525 specification provides only a general method of producing [**22] human insulin cDNA and a description of the human insulin A and B chain amino acid sequences that cDNA encodes, it does not provide a written description of human insulin cDNA. Accordingly, the district court did not err in concluding that claim 5 is invalid for failure to provide an adequate written description."* (Examiner quoted text in bold)

In *Lilly*, the patents at issue related to recombinant DNA technology and specifically to plasmids and microorganisms that produce human insulin. Although the specification provided a written description of rat cDNA, it did not provide an adequate written description of human cDNA to thereby support the claims. Simply stated, because of the redundancy of the genetic code, the information provided in the specification did not allow the ordinary practitioner to surmise the, then unknown, structure of human cDNA, needed to produce the human insulin. Thus, the court concluded that a specification that only describes known rat cDNA did not provide an adequate written description of unknown human cDNA, at least for the purposes of claiming plasmids and microorganisms that produce human insulin and thereby precluding others from possessing the claimed subject matter during the term of the patent.

In the present case, the Final Action tersely concludes that: "*A review of the specification fails to find adequate written description of any molecular probe and binding partner that are to be used in the claimed invention.*" (Final Action at paragraph 7, page 8). However, this asserted fact has been proven to be false since the specification specifically defines "molecular probe" and "binding partner" and Example 1 provides concrete embodiments of these entities. Further reference is made to page 23, line 5, to page 24, line 25 of the specification

wherein there a discussion of how to select possible molecular probes and binding partners.

Moreover, References **CS, DB, DC, DE, DF, DH, DI, DJ, DL, DO, DS, DT** and **DU** (as discussed above) teach that molecular probes and "immuno-probes" (i.e. binding partners such as antibodies) are well-known and often used for the purposes described in the specification. Specifically, these compositions are known to exhibit predicable binding specificity properties that can be used to identify organisms at various taxonomic levels. Thus, unlike the situation in *Lilly*, the present specification specifically describes embodiments of the claim elements in terms of known compositions (i.e. nucleic acid or peptide nucleic acid probes and antibody/antigen interactions) that exhibit the properties required for practice of the claimed methods. This fact is also supported by statements in the specification, such as those in the "Background" section. Consequently, there is simply no similarity between the facts of *Lilly* and the disclosure of the present invention. Consequently, Appellants contend that the Office's reliance on *Lilly* to reject the present claims is misleading, the analysis is incomplete and the conclusions of the Final Action based thereon are erroneous.

In addition to the foregoing, Applicants wish to make of record the very recent decision in *Capon v. Eshhar*, 418 F.3d 1349, 76 U.S.P.Q.(BNA) 1078 (Fed. Cir. 2005) (hereinafter "*Capon*"). In *Capon*, it was held that there is no requirement that the nucleotide sequences of chimeric genes must be fully presented where the component DNAs are known. Importantly, the decision in the *Capon* was distinguished from the *Lilly* and *Rochester* decisions upon which the Office has placed so much reliance in articulating the present rejection. Simply stated, the *Capon* situation is much closer to the present facts than is either of *Lilly* or *Rochester* situations because in the present situation, the claim limitations "molecular probe" and "binding partner" are expressly disclosed and defined within the specification and they are embodied by known compositions that are being used in the manner that they are ordinarily used the art (i.e. as

"molecular" and "immuno" probes that bind to other compositions with some degree of specificity and predictability).

In summary, the arguments and asserted "facts" are believed to be insufficient to support a proper rejection under 35 U.S.C. §112, first paragraph for lack of written description. Withdrawal of the rejection by the Board is earnestly requested.

(v) Rebuttal To The Advisory Action

It is respectfully submitted that the Final Action and the Advisory Action fail to supply any "facts" that support a conclusion that the present application lacks a proper written description. Moreover, the Office cannot ignore the teachings of the specification and/or references cited therein simply by suggesting that they are the "opinion" of Appellants' representative.

In response to Appellants' reference to the definitions of "molecular probe" and "binding partner" in the specification and the related arguments at pages 17-19 of Appellants' submission of September 20, 2005, the Advisory Action states:

> *"The specification has not provided an adequate written description of those members of the various groups such that one would be able to identify which [sic] a high degree of confidence, just which nucleic acid would best serve as a probe, or a target or which antibody would best serve to bind an antigen of interest."* (Advisory Action at continuation sheet page 1, paragraph 6)

With all due respect, it has never been a requirement that Appellants specify every conceivable detail of every possible experiment that any skilled artisan may ever perform within the scope of the claimed invention.[3] All that is required of the

3 In *Capon*, the court stated: "The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in predictability of the science. *Capon v. Eshhar,* 418 F.3d 1349, 1357, 76 U.S.P.Q.(BNA) 1078, 1084 (Fed. Cir. 2005)

written description is that the specification provide the ordinary practitioner with a description sufficient to understand how to practice the claimed invention wherein it is assumed that the ordinary practitioner is competent to apply known methods and procedures such as those described in References **CS, DB, DC, DE, DF, DH, DI, DJ, DL, DO, DS, DT** and **DU** (as discussed above). Since the argument quoted above rests upon a misunderstanding of the law, the rejection is *prima facia* deficient. Since it is deficient, the rejection should be withdrawn.

The error of this argument can be illustrated with a hypothetical situation where, for example, an application claims a new method for hanging a door on a door jamb and it involves the use of screws, hinges and a screwdriver. It is presumed that a carpenter (one of skill in the art) will appreciate how to select the proper screws, screwdriver and hinges to practice the claimed method for a particular application (i.e. a big door or a smaller door) even if it takes some routine trial and error so long as it is routine and commonly practiced.

This hypothetical situation is highly analogous to the above quoted basis for the present rejection. All the presently pending claims are method claims. Without any basis whatsoever, the quote suggests that the ordinary practitioner needs guidance in selecting specific probes, targets and antibodies (Advisory Action at page 1, paragraph 6) for any and all specific applications. This is analogous to saying that because he is incompetent to perform such a task, the carpenter cannot select the proper screwdriver, screws and hinges to practice the disclosed method of hanging the door on the door jamb. If this were the law it would lead to multi-hundred page specifications (a situation most Examiner's would object to). But, as stated above, the asserted basis for this rejection expresses a misunderstanding of both the state of the art as well as the requirements of the law.

With respect to the state of the art, Reference **DB** specifically contradicts the "factual" assertion by stating:

"This combination of rRNA-targeted hybridization probes and

*immuno-probes for flow cytometry makes possible the highly specific and automated identification of micro-organisms at any desired taxonomic level" (emphasis added, Reference **DB**, under the heading "Summary" on page 569)*

This reference also specifically states:

"In this study we describe the simultaneous use of rRNA targeted probes, which are in general specific at the species level and above, and antibodies, which are frequently specific at the species level and below. The combination of these two highly specific molecular tools opens up the whole range of phylogenetic levels for the high resolution and automated identification of micro-organisms by flow cytometry. (Reference DB, at page 570, col. 1, lines 41-48)

Thus, this reference leads to the conclusion that choosing "molecular" and "immuno-probes" for the determination of mirco-organisms at any taxonomic level is within the ability of the ordinary practitioner. Because the "factual" assertion upon which the rejection relies is contradicted by References in the record it is clear error. Therefore, Appellants submit that when the knowledge of one skilled in the art (as demonstrated by the content of various References) in considered in view of the teachings of the specification, adequacy of the present written description is demonstrated and the Office has failed to establish any facts to the contrary.

Next, the Advisory Action states:

"... claim 1 requires the use of a "molecular probe" that when bound to a target organism, a binding partner immobilized on a solid support will also bind only to those organisms where the molecular probe has been bound. In the case of a nucleic acid probe, which hybridizes to nucleic acid in the nucleus of a cell, the immobilized binding partner must somehow be able to reach all the way through the cell and into the nucleus, find the complex of nucleic acid probe – target nucleic acid, bind to it, all the while remaining immobilized to the external support. Clearly, even of this date, no such mechanism is known. A review of the specification is similarly silent as to how this most remarkable feat is to be accomplished". (Advisory Action at

continuation sheet page 1, paragraph 7)

While it would be quite a remarkable feat for a surface bound ligand (e.g. nucleic acid) to interact with molecules in the nucleus of an organism or cell, the simple rebuttal is that this argument rests on an incorrect premise. Nowhere in the claims or specification is there any suggestion or requirement that the support bound binding partner must interact with any molecule beyond the surface of the cell or organism for the method to operate. For example, it is well-known that nucleic acids exhibit a wide variety of interactions and that cell surfaces comprise numerous moieties with which all kinds of molecules interact, including nucleic acids. In Example 1, antibody binding partners that are support bound are used to immobilize organisms as the antigen by reacting with the surface of the "antigen" cell/organism (See: Specification at page 33, lines 9-10 and Example 1). The assumption being clear error, arguments relying thereon cannot support the present rejection.

Next, the Advisory Action states:

> "*As set forth at page 7 of the Office action, claim 12 specifically requires the use of "molecular probes [that stain] all organisms of a domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain without regard to whether or not this represents the organism of interest and wherein the binding partner is specific for the domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain that is the organism of interest." The specification does not provide adequate written description of such compounds, much less an indication [sic] which compounds work best (or at all) with another.*" (Advisory Action at page 1, paragraph 8)

Again, without any basis whatsoever, a claim has been made that contradicts the teachings of the art. As stated above, Reference **DB** states that by combining nucleic acid probes (i.e. a molecular probe) and "immuno-probes" (i.e. a binding partner such as an antibody) it is possible

to achieve specificity "*at any desired taxonomic level*". The premise of this argument being disproved, the conclusion is improper support for the present rejection.

Next, the Advisory Action refers to another section of the *Lilly* decision. (Advisory Action at continuation sheet page 1, paragraph 9 to bridging paragraph 10 and continuation sheet 2 (paragraph 11)). Based upon this citation, the Examiner then argues: "*Here, as in Lilly, the claims at issue comprise language that define the "molecular probe" and "binding partner" in terms of how they are to function, or the desired result that is to be achieved.*" (Advisory Action at continuation sheet, page 2).

Appellants reiterate that the Office's reliance upon *Lilly* exhibits a misunderstanding of both the facts and the law. As stated above, unlike the case in *Lilly*, the present claims rely on the manipulation of known entities (e.g. nucleic acid probes, PNA probes and antibodies) that are often used by the ordinary practitioner to identify organisms at various taxonomic levels. That is what references cited in the file actually teach (It is not mere opinion of Appellants' representative). Moreover, any reliance on *Lilly* is misplaced since the claims in *Lilly* were drawn to new compositions (i.e. a gene), not to new methods. Accordingly, this quote from *Lilly* is irrelevant to the presently claimed subject matter because, all presently pending claims are method claims and, as is well-documented in the specification and in the references discussed herein, all of the composition elements of said method claims are based upon known entities which are used in the manner in which they are commonly used in the art. Accordingly, it is respectfully submitted that any reliance upon *Lilly* to support the present rejection is not well grounded in fact or law.

Next, the Advisory Action argues that unlike *Capon*, the present set of facts are more akin to *Lilly* because there is no expert testimony supporting Appellants' position. Appellants reiterate that for reasons previously argued, *Capon* is more relevant to the present set of facts than

is *Lilly*. Furthermore, the law is clear that the specification is presumed to be adequate as of filing date and the Office bears the burden to present facts that support a conclusion that it lacks a proper written description. Since no facts have been established to support the present rejection, no expert opinion (i.e. declaration) is required to rebut the Office's assertions. Finally, because all of the asserted facts have been proven to be incorrect, and all the Office's reliance upon caselaw demonstrated to be off-point, misplaced and/or irrelevant, it is respectfully submitted that no basis exists for rejecting claims 1-50. Withdrawal of the rejection is therefore requested.

(vi) Section Summary

In summary, it is respectfully submitted that the specification complies with the written description requirement and that in any event the Office has not provided any facts that demonstrate the contrary. Accordingly, Appellants believe that the present rejection under 35 U.S.C. § 112, first paragraph, written description, should be withdrawn. Reversal of the Examiner's error is earnestly solicited.

C. Rejection Under 35 U.S.C. § 112, First Paragraph For Lack Of Enablement

(a) The Law

"The purpose of the enablement requirement is to ensure that the invention is communicated to the interested public in a meaningful way." M.P.E.P. § 2164 "However, to comply with 35 U.S.C.§ 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim to that effect."" *Id.* "Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention." *Id.*

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." M.P.E.P. § 2164.01 "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." *Id.*

(b) Analysis of The Rejection In View Of The Law

(i) The Factual Assertions Supporting the Rejection are Erroneous

Paragraph 10 of the Final Action quotes from "*Enzo Biochem Inc. v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135 bridging to 1136" and asserts that the specification fails to enable one of skill in the art to make and/or use the invention (Final Action at page 9). However, the discussion offers no analysis of any facts that support this conclusion. Consequently, the significance of this paragraph of the rejection is not well stated and requires no reply by Appellants.

Paragraph 11 of the Final Action begins by arguing that Appellants don't possess the invention and therefore cannot have enabled it. (Final Action at page 9-10) As discussed above, the premise of this argument is without merit. Specifically, Appellants' specification demonstrates possession of the invention. It being based upon an incorrect premise, the conclusion of the argument cannot be correct.

The Advisory Action then states: "... *the specification does not provide the essential starting materials or reaction conditions that must be employed when practicing the claimed invention.*" (OA at page 9-10) This too is incorrect for the reasons discussed above. Further reference is made to Example 1 (beginning at page 35). In this example, it was demonstrated that a commercially available coded bead comprising a linked Salmonella specific antibody was able to specifically capture the "stained" detectable *S. choleraesuis* wherein the bacteria were stained with fluorescently labeled PNA probes. Accordingly, this Example

demonstrates both possession of the invention and disproves any contention that no specific starting materials or reaction conditions have been disclosed by Appellants. The factual basis of the asserted rejection having been disproved, it should be withdrawn.

Regarding the reference to "essential conditions", method claims 1, 18 and 35 contain the claim limitations for each method and the Examiner has failed to describe how any of the disclosed limitations are deficient. Further reference is made to pages 16-17 wherein there is a discussion of such topics as: "Hybridization Conditions/Stringency", "Suitable Hybridization Conditions", "Suitable Antibody Binding Conditions" and "Harmonization Of Suitable Hybridization Conditions & Suitable Antibody Binding Conditions". Clearly these discussions provide direction to the ordinary practitioner with respect to operation of the methods of the invention. The Examiner is reminded that: 1) "The test of enablement is whether one reasonably skilled in the art could make or use the invention **from the disclosures in the patent** (emphasis added) coupled with information known in the art without undue experimentation." M.P.E.P. § 2164.01 and that: 2) "Detailed procedures for making and using the invention **may not be necessary** (emphasis added) if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention." M.P.E.P. § 2164.

In the present case, References **CS, DB, DC, DE, DF, DH, DI, DJ, DL, DO, DS, DT** and **DU** (as discussed above) demonstrate that much is known to the ordinary practitioner about how to select and use "molecular" and "immuno"-probes to determine all kinds of organisms and that such selections can be reasonably predicable for determining organisms at all taxonomic levels. Consequently, any assertion that what the art teaches are merely the opinions of "applicant's representative" (Final Action at paragraph 11, pages 11-12), is incorrect since what a reference teaches is a matter of fact. *In re Bell*, 991 F.2d 781, 784, 26 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1993). Consequently, the Office's failure to explain why the various references cited in the Information Disclosure

Statements and further discussed herein fail to establish sufficient knowledge in the ordinary practitioner to practice the invention as described in the specification and claims is obvious error.

(ii) Statements In The Specification Have Been Misinterpreted

Paragraphs 12-13 (pages 10-11) of the Final Action take statements made in the background of the specification out of context and thereby mischaracterize that discussion. The relevant paragraph of the background section of the specification reads:

> *"Nucleic acid hybridization is a fundamental process in molecular biology. Probe-based assays are useful in the detection, quantitation and/or analysis of nucleic acids. Nucleic acid probes have long been used to analyze samples for the presence of nucleic acid from bacteria, fungi, virus or other organisms and are also useful in examining genetically-based disease states or clinical conditions of interest. Nonetheless, nucleic acid probe-based assays have been slow to achieve commercial success. This lack of commercial success is, at least partially, the result of* ***difficulties associated with specificity, sensitivity and/or reliability****."* (bold text quoted by the Examiner)

This quoted paragraph affirmatively states that nucleic acid hybridization is recognized as a fundamental process in molecular biology and that it has long been applied but that it possesses certain deficiencies that make it less than ideal for some commercial applications. The statement does not lead to the conclusion that nucleic acid hybridization is: "*wrought with "difficulties associated with specificity, sensitivity, and/or reliability*" in a general sense. It merely indicates that there is room for improvement that could lead to more specific, sensitive and reliable assays at various taxonomic levels. This point of view is generally echoed in Reference **DB**.

That nucleic acid probes can be used for the identification of micro-organisms (e.g. bacteria) is also evident from the various references submitted in the Information Disclosure Statements in the application file and discussed herein

and is specifically supported by the text quoted above from Applicants' specification (See in particular: all reference herein to Reference **DB** wherein it has been specifically stated that the combination of nucleic acid probes and "immuno-probes" (i.e. antibodies) can facilitate the "*identification of micro-organisms at any desired taxonomic level*") (Abstract of Reference **DB**). Also, the specification discloses that the combination approach (combining "molecular probes" and "binding partners") leads to improvements in specificity (Specification at page 21, line 31 to page 22, line 7) as compared with the use of such nucleic acid probes alone.

Moreover, "*...to comply with 35 U.S.C.§ 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim to that effect.*"" M.P.E.P. § 2164. Consequently, that nucleic acid probes can sometime exhibit certain difficulties associated with specificity, sensitivity and/or reliability" that might preclude their use in commercial products does not preclude their use in the present invention. Consequently any assertion that Appellants' statement that nucleic acids don't make the best commercial "molecular probes" when used alone to support a finding of lack of enablement requirement is inconsistent with the law and with the facts.

In the final sentence of paragraph 12 of the Advisory Action states: "*Even if the claims were to be limited to PNA probes, the specification does not teach which probes are to be used, much less which probes are to be used in combination with various molecular probes so that every "species, taxon, subclass, subspecies, serotype, or strain" of the organisms can be identified.*" It seems that by this statement, the Office expects Appellants to list every probe sequence that could ever be used to determine each and every specific organism that can ever be determined. It suffices to say that no such requirement exists under the law. (Also see the discussion above pertaining to the hypothetical and the carpenter's selection of hinges, screws and a screwdriver) This is clear

because, "*The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.*" M.P.E.P. § 2164.01 That the selection of "molecular probes" and "immuno-probes" for particular applications is within the ability of the ordinary practitioner is fully supported by the prior quotations from Reference **DB**. Additionally, as stated in the background:

> *"Nucleic acid hybridization is a fundamental process in molecular biology. Probe-based assays are useful in the detection, quantitation and/or analysis of nucleic acids. Nucleic acid probes have long been used to analyze samples for the presence of nucleic acid from bacteria, fungi, virus or other organisms and are also useful in examining genetically-based disease states or clinical conditions of interest."* (Specification at page 2)

Since the Examiner has not contested the accuracy of this statement, it is clear that the production of suitable probes is well understood and need not be specifically described in detail in the specification for every conceivable application. Moreover, "*The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation.*" M.P.E.P. § 2164.01 That the art does routinely engage in such experimentation is demonstrated by the various References **CS, DB, DC, DE, DF, DH, DI, DJ, DL, DO, DS, DT** and **DU** (as discussed above). Accordingly, there is simply no requirement under 35 U.S.C. 112, first paragraph that every conceivable probe sequence, target sequence and related organism be expressly stated in the specification since the preparation of the requisite probes and binding partners is well understood and practiced in the art and the assertion that such disclosure is required is erroneous. It being clear that the Final Action provides no facts that support the rejection, withdrawal of the rejection is requested.

(iii) Rebuttal To The Advisory Action

The final paragraph of the continuation sheet of the Advisory Action appears to reiterates that this rejection rest largely on the prior finding that the present specification lacks a proper written description. For the reasons already argued, this conclusion is wrong. That this conclusion is clear error is also apparent with reference to Example 1, wherein a representative assay was performed. Accordingly, for at least this reason, it is believed that the present rejection of claims 1-50 under 35 U.S.C. §112, first paragraph for want of enablement should be withdrawn.

With respect to the Examiner's assertions that Appellants have attempted to shift the burden of enablement to the public, it suffices to say that no established facts support the argument that the present specification is deficient according to the law. Withdrawal of the rejection is therefore requested.

(iv) Section Summary

In summary, the premises of the arguments supporting the rejection being incorrect and unsupported by established fact, it is respectfully submitted that the rejection for lack of enablement under 35 U.S.C. § 112, first paragraph should properly be withdrawn. Reversal of the Examiner's position is earnestly solicited.

Summary

Because all arguments supporting the final rejection are clear error, it is respectfully requested that this honorable Board of Patent Appeals and Interferences reverse the Examiner's decision in this case and indicate the allowability of all pending claims.

In the event that this paper is not being timely filed, Appellant respectfully petitions for an appropriate extension of time. Any fees for such an extension together with any additional fees that may be due with respect to this paper may be charged to Counsel's Deposit Account 01-2213.

Respectfully submitted
On behalf of Appellants

March 13, 2006
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8. APPENDIX A

Claims on appeal

1. (Original) A method for determining an organism of interest in a sample from another organism or organisms to be distinguished; said method comprising:

treating the sample, or a portion thereof, with at least one detectable molecular probe wherein the molecular probe or probes are selected such that either:

(i) both the organism of interest and the other organism or organisms react with the molecular probe in a way that produces detectable organisms of interest and a detectable other organism or organisms to be distinguished; or

(ii) only the organism of interest reacts with the molecular probe in a way that produces only detectable organisms of interest; and

contacting the sample, or a portion thereof, with a solid carrier to which has been immobilized a binding partner such that if (i) applies then the binding partner is chosen to be reactive only with the detectable organism of interest but not reactive with the detectable other organism or organisms to be distinguished; but if (ii) applies then the binding partner is chosen to be generally reactive with the detectable organism of interest but also may be reactive with the other organism or organisms to be distinguished; and

determining the presence, absence, position or number of detectable organisms immobilized to the solid carrier and correlating the result with the presence, absence, or number of the organisms of interest in the sample, or portion thereof.

2. (Original) The method of claim 1, wherein the detectable molecular probe

is selected from the group consisting of a nucleic acid and a non-nucleic acid.

3. (Original) The method of claim 2, wherein the non-nucleic acid is a peptide nucleic acid.

4. (Original) The method of claim 1, wherein the detectable molecular probe is not labeled with a detectable moiety.

5. (Original) The method of claim 4, wherein the detectable molecular probe is detected using a detectable antibody that specifically binds to a detectable molecular probe/target sequence complex.

6. (Original) The method of claim 5, wherein the detectable molecular probe is an unlabeled peptide nucleic acid.

7. (Original) The method of claim 1, wherein the detectable molecular probe is labeled with a detectable moiety.

8. (Original) The method of claim 7, wherein the detectable moiety is selected from the group consisting of: a chromophore, a fluorochrome, a spin label, a radioisotope, an enzyme, a hapten and a chemiluminescent compound.

9. (Original) The method of claim 1, wherein the binding partner is an antibody.

10. (Original) The method of claim 1, wherein the binding partner is selected from the group consisting of: a carbohydrate, a lectin, a peptide, a receptor, a charged polymer and a protein.

11. (Original) The method of claim 1, wherein the solid carrier is selected from the group consisting of: a particle, a bead, a microscope slide, a micro titre plate, a membrane and an array.

12. (Original) The method of claim 1, wherein the molecular probe stains all organisms of a domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain without regard to whether or not this represents the organism of interest and wherein the binding partner is specific for the domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain that is the organism of interest.

13. (Original) The method of claim 1, wherein the molecular probe stains only the domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain that is the organism of interest and wherein the binding partner is specific for a particular domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain without regard to whether or not this represents the organism of interest.

14. (Original) The method of claim 1, wherein the molecular probe stains only the domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain that is the organism of interest and wherein the binding partner is specific for only the domain, kingdom, group, class, genus, species, taxon, subclass, subspecies, serotype or strain that is the organism of interest thereby providing an assay that provides certainty at two different levels of molecular discrimination.

15. (Original) The method of claim 1, wherein the sample, or portion thereof, is treated with the detectable molecular probe or probes before being contacted with the solid carrier.

16. (Original) The method of claim 1, wherein the sample, or portion thereof, is contacted with the solid carrier before being treated with the detectable molecular probe or probes.

17. (Original) The method of claim 1, wherein the sample, or portion thereof, is simultaneously contacted with both the solid carrier and treated with the detectable molecular probe or probes.

18. (Original) A method for sorting and determining an organism or organisms of interest in a sample or samples; said method comprising:

treating the sample or samples, or a portion thereof, with one or more detectable or independently detectable molecular probes wherein the one or more molecular probes are selected such that either:

(i) the detectable probe or probes react with the different organisms to be determined in a way that produces different detectable organisms that possess the same stain; or

(ii) the independently detectable probes react with the different organisms to be determined in a way that produces different independently detectable organisms that possess an independently detectable stain; and

contacting the sample or samples, or a portion thereof, with one or more different types of coded beaded supports, wherein each different type of coded beaded support can be independently determined in a suitable particle sorter and wherein to the coded beaded supports have been immobilized one or more binding partners chosen to select a particular organism or organisms such that the detectable or independently detectable organisms become selectively bound to the coded beaded supports as a result of the occurrence of specific binding partner interactions;

sorting the different types of coded beaded supports in a suitable particle sorter; and

determining the presence, absence, or number of detectable organisms, or each of the independently detectable organisms, immobilized to each different type of coded beaded support and either: (iii) correlating the result with the particular binding partner immobilized to each particle type to thereby determine the presence, absence or number of each of the different organisms of interest in the sample, or portion thereof; or (iv) correlating the result with the code for a sample source from which the sample, or portion thereof, was derived to thereby determine the presence, absence or number of each of the different organisms of interest in each different sample, or portion thereof.

19. (Original) The method of claim 18, wherein the detectable molecular probe is selected from the group consisting of a nucleic acid and a non-nucleic acid.

20. (Original) The method of claim 19, wherein the non-nucleic acid is a peptide nucleic acid.

21. (Original) The method of claim 18, wherein the detectable molecular probe is not labeled with a detectable moiety.

22. (Original) The method of claim 21, wherein the detectable molecular probe is detected using an detectable antibody that specifically binds to a detectable molecular probe/target sequence complex.

23. (Original) The method of claim 22, wherein the detectable molecular probe is an unlabeled peptide nucleic acid.

24. (Original) The method of claim 18, wherein the detectable molecular probe is labeled with a detectable moiety.

25. (Original) The method of claim 24, wherein the detectable moiety is selected from the group consisting of: a chromophore, a fluorochrome, a spin label, a radioisotope, an enzyme, a hapten and a chemiluminescent compound.

26. (Original) The method of claim 18, wherein the independently detectable probes are labeled with independently detectable fluorophores.

27. (Original) The method of claim 18, wherein the particular binding partner is an antibody.

28. (Original) The method of claim 18, wherein the binding partner is selected from the group consisting of: a carbohydrate, a lectin, a peptide, a receptor, a charged polymer and a protein.

29. (Original) The method of claim 18, wherein the sample, or portion thereof, is treated with the detectable or independently detectable molecular probe or probes before being contacted with the solid carrier.

30. (Original) The method of claim 18, wherein the sample, or portion thereof, is contacted with the solid carrier before being treated with the detectable or independently detectable molecular probe or probes.

31. (Original) The method of claim 18, wherein the sample, or portion thereof, is simultaneously contacted with both the solid carrier and treated with the detectable or independently detectable molecular probe or probes.

32. (Original) The method of claim 18, wherein the detectable molecular probe or probes stain all of the different organisms with the same stain and wherein the binding partner is specific for each of the different organisms of interest such that the sorting of the different types of coded beaded supports determines each of the different organisms of interest in the sample, or portion thereof, based solely upon the identity of the different binding partner.

33. (Original) The method of claim 18, wherein the independently detectable molecular probe or probes stain all of the organisms of interest provided that some or all of the different organisms of interest are stained differently and wherein each binding partner associated with each different type of coded beaded support is chosen to select among the same or differently stained organisms such that the sorting of the different types of coded beaded supports when considered in combination with the stain of the organism or organisms bound to each different type of coded beaded support determines each of the different organisms of interest in the sample, or portion thereof.

34. (Original) The method of claim 18, wherein the independently detectable molecular probes stain the organism or organisms of interest differently and wherein each binding partner associated with each different type of coded beaded support is generic to the chosen assay but each different coded beaded support codes for a different sample such that the determination of the stain or stains on each different coded beaded support specifically determines each of the one or more organisms of interest in the sample, or portion thereof, and each different coded beaded support identifies the source of the sample, or portion thereof.

35. (Original) A method for sorting and determining different organisms of interest in a sample; said method comprising:

treating the sample, or a portion thereof, with one or more detectable or independently detectable molecular probes wherein the one or more molecular probes are selected such that either:

(i) the detectable probe or probes react with the different organisms to be determined in a way that produces different detectable organisms that possess the same stain; or

(ii) the independently detectable probes react with the different organisms to be determined in a way that produces different independently detectable organisms that possess an independently detectable stain; and

contacting the sample, or a portion thereof, with a solid carrier array to which binding partners have been immobilized at unique identifiable locations such that the detectable or independently detectable organisms are selectively bound to the locations on the array as a result of the occurrence of specific binding partner interactions; and

determining the presence, absence or number of the detectable or independently detectable organisms immobilized at the many different locations of the array and correlating the result with the particular binding partner immobilized to each location on the array to thereby determine the presence, absence or number of the different organisms of interest in the sample.

36. (Original) The method of claim 35, wherein the detectable molecular probe is selected from the group consisting of a nucleic acid and a non-nucleic acid.

37. (Original) The method of claim 36, wherein the non-nucleic acid is a peptide nucleic acid.

38. (Original) The method of claim 35, wherein the detectable molecular probe

is not labeled with a detectable moiety.

39. (Original) The method of claim 38, wherein the detectable molecular probe is detected using a detectable antibody that specifically binds to a detectable molecular probe/target sequence complex.

40. (Original) The method of claim 39, wherein the detectable molecular probe is an unlabeled peptide nucleic acid.

41. (Original) The method of claim 35, wherein the detectable molecular probe is labeled with a detectable moiety.

42. (Original) The method of claim 41, wherein the detectable moiety is selected from the group consisting of: a chromophore, a fluorochrome, a spin label, a radioisotope, an enzyme, a hapten and a chemiluminescent compound.

43. (Original) The method of claim 35, wherein the independently detectable probes are labeled with independently detectable fluorophores.

44. (Original) The method of claim 35, wherein the binding partner is an antibody.

45. (Original) The method of claim 35, wherein the binding partner is selected from the group consisting of: a carbohydrate, a lectin, a peptide, a receptor, a charged polymer and a protein.

46. (Original) The method of claim 35, wherein the sample is treated with the detectable or independently detectable molecular probe or probes before being contacted with the solid carrier.

47. (Original) The method of claim 35, wherein the sample is contacted with the solid carrier before being treated with the detectable or independently detectable molecular probe or probes.

48. (Original) The method of claim 35, wherein the sample is simultaneously contacted with both the solid carrier and treating with the detectable or independently detectable molecular probe or probes.

49. (Original) The method of claim 35, wherein the detectable molecular probe or probes stain all of the different organisms with the same stain and wherein the binding partner is specific for each of the different organisms of interest such that the sorting of the organisms on the array resulting from the binding partner interactions occurring at the unique locations is used to thereby determine each of the different organisms of interest in the sample, or portion thereof, based solely upon the identity of the different binding partners at the unique locations.

50. (Original) The method of claim 35, wherein the independently detectable molecular probe or probes stain all of the organisms of interest provided that some or all of the different organisms of interest are stained differently and wherein each binding partner associated with a unique location on the array is chosen to select among the same or differently stained organisms such that the sorting of the organisms on the array resulting from the binding partner interactions occurring at the unique locations, when considered in combination with the stain of the organism or organisms bound to each unique location, is used to determine each of the different organisms of interest in the sample, or portion thereof.

Appendix B - Evidence Under §§ 1.130, 1.131 or 1.132

Appendix C – Related Proceedings